are unimproved and 76 per cent. are either greatly improved or well. This study, however, has shown that the postoperative sinuses of the patients on whom nephro-ureterectomies were performed healed in an average time of five months, whereas the women in whom the diseased ureters were left, drained for eleven months. From this it would appear that it is better to remove the ureter along with the kidney when the condition of the patient warrants prolonging the anesthetic the short time necessary for carrying out this procedure.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Studies on Experimental Pneumonia.—The experimental study of lobar pneumonia has long been hampered by the difficulty surrounding the production of this disease in animals. The various attempts at introducing bacteria into the deeper air passages by insufflation and by injection in fluid suspension have resulted in bronchopneumonias. Even the highly artificial method of flooding the lung with a suspension of bacteria failed to produce the typical lobar pneumonia. Following a method used by Opie and others in unpublished experiments, BLAKE and CECIL (i, *Jour. Exper. Med.*, 1920, xxxi, 403) were able to produce typical lobar pneumonias in monkeys. The method was by inserting a dry, sterile needle into the trachea and injecting very small doses of living, virulent pneumococci. The organisms were always suspended in 1 c.c. of fluid. All the biological types of pneumococci were employed. The following is a brief summary of the results obtained with the different biological groups of pneumococci: Out of 31 monkeys injected with type, i, 26 took lobar pneumonia. Out of 2 monkeys injected with type ii, 2 took lobar pneumonia. Out of 3 monkeys injected with type iii, 3 took lobar pneumonia. Out of 4 monkeys injected with type iv, 1 took lobar pneumonia. All monkeys injected with types ii, iii and iv recovered. Out of 6 monkeys exposed to contact infection only 1 developed lobar pneumonia. Inoculation of pneumococci into the nose and throat induced a carrier state but none of these animals contracted lobar pneumonia, nor did they develop any infection of the upper respiratory tract. Subcutaneous and intravenous injection of pneumococci did not produce lobar pneumonia. Invasion of the blood stream by pneumococci was demonstrated to be secondary to the infection of the lung. They have shown, therefore, that lobar pneumonia is bronchiogenic in origin. Pneumococci were isolated from the blood stream within six hours after the intratracheal

injection. The methods of study after inoculation were similar to the ordinary clinical methods. They consisted in observation and record of clinical symptoms and physical signs, with temperature records made twice daily and daily white cell and differential blood counts, and blood cultures. These records were in every way comparable to those obtained in the course of a lobar pneumonia in the human. Autopsies on the animals that died and on others killed at selected intervals furnished the material for the experimental study of the pathology of the disease. In the report of this work (ii, *Jour. Exper. Med.*, 1920, xxxi, 445) is included the study of 40 autopsies on monkeys. Of these 27 died during the active stage of the disease, or from complications, and 13 were killed at varying intervals following the crisis. This series of animals permitted study of the lungs at intervals of one to twenty-three days after the onset of the disease. This series presented examples of the four classical stages of the disease. Animals dying within five days after intratracheal injection showed either engorgement or red hepatization. The later stages have been thoroughly studied in human material. It is from the study of the early stages that this phase of the problem attains its chief interest. Microscopic examination showed that while the infection invades by the bronchiogenic route, it soon becomes interstitial at some point near the hilus of the lung, producing an early, acute inflammatory reaction in the vascular adventitia and walls of the bronchi near the root of a lobe. This is accompanied by edema and a leukocytic infiltration of the interstitial tissues and by intense capillary engorgement. At this stage bacteria were found to spread rapidly throughout the lung, following the ramifications of the vascular and bronchial trees and appearing always to precede cellular exudation into the alveoli. In the same way hepatization was found to spread throughout the lobe from the region of the hilus to the periphery. During this early process the epithelium of the bronchial tree appears fairly intact and the air passages contain little or no exudate. After the five-day period, in which time the stage of red hepatization has developed, the more familiar histological pictures of lobar pneumonia appeared. The earliest exudate in the alveoli consisted of a few large mononuclear cells and quantities of coagulated serum. Polymorphonuclear leukocytes, more large mononuclear phagocytic cells, and red blood cells are shortly added to this and appear imbedded in a meshwork of fibrin. The red color of the lung would appear from these studies to be largely due to the engorged capillaries than to free blood. At this time the interstitial lesions were much less prominent than before red hepatization had occurred. The margins of the advancing consolidation continued to show a primary interstitial character of the lesion, and the lumina of terminal bronchioles at the margin were clear of exudate while those lying within the consolidated area contained an exudate like that found in the alveoli. The transition from red to gray hepatization began in the oldest areas of consolidation near the hilus. The picture here was the familiar one so often encountered in lobar pneumonia. At this stage the interstitial reaction had become much less conspicuous. And, as is true in lobar pneumonia in the human, necrosis of the alveoli structure and air passages and thrombosis of vessels were not found. The animals dying late in the disease, or killed shortly after clinical recovery, showed the alveolar exudate to be

undergoing rapid disintegration. It was in every way similar to the picture of resolving pneumonin in the human. Finally it was interesting to note that along with resolution a variable degree of organization was always found. This was present in the perivascular tissues though variable in amount, and likewise to some degree about the bronchi. There were some instances of organization of the exudate. The newly formed fibrous tissue was found covered by a thin layer of epithelium apparently derived from the alveolar lining. The pathogenesis of lobar pneumonia as described by these authors is best followed by briefly reviewing their findings as to the presence of pneumococci in the tissues. While pneumococci were never found in the air passages save after the development of red hepatization in the surrounding tissues, they were demonstrated beneath the bronchial epithelium and in the peribronchial and perivascular stroma three hours after an intratracheal injection. Further, in 2 monkeys, with abortive attacks of pneumonia (recovery on third and fourth days respectively), autopsies immediately after recovery showed a purely interstitial pneumonia without hepatization. The spread of pneumococci from the initial site of invasion of the interstitial tissues near the hilus was entirely by interstitial tissues and lymphatics as far as the alveolar walls where they may be seen prior to an exudation into alveoli. And pneumococci were found free in alveoli as soon as the serous exudate appeared there, and before there was any cellular exudate. They therefore preceded any development of hepatization. During the progress of the above work a considerable amount of spontaneous pneumonia occurred among the stock monkeys. (iii, *Jour. Exper. Med.*, 1920, xxxi, 499). Where possible these were studied clinically and autopsies were performed in all fatal cases, the bacteriological findings in heart's blood, lung, and bronchi being worked out at the same time. It is interesting and definitely in support of the experimental method, to note that spontaneous lobar pneumonia in monkeys is identical with that produced by intratracheal injection of pneumococci, and with lobar pneumonia in man. The outbreak further was shown to have epidemiological interest in that it illustrated how the spread of infection by contact may be accomplished when conditions are favorable. In conjunction with the production of experimental pneumonia in monkeys, Blake and Cecil (iv, *Jour. Exper. Med.*, 1920, xxxi, 519) studied the results of prophylactic vaccination against pneumococcus pneumonia in monkeys. Both saline vaccine and lipovaccine made from a strain of pneumococcus type i were employed. The former gave better results; at least it appeared to have a favorable action in preventing pneumococcus septicemia. No protection was afforded by either type of vaccine against subsequent attacks of pneumococcus pneumonia, and no cross protection against other types of pneumococcus could be demonstrated. The development of active immunity against experimental pneumococcus pneumonia in monkeys following vaccination with living cultures of pneumococci was also tried (v, *Jour. Exper. Med.*, 1920, xxxi, 657). This method has been shown by various workers to have some success against other pathogenic bacteria, and the facility with which monkeys could be exposed to experimental pneumococcus pneumonia made them an excellent subject for the study of the method in pneumococcus infection. Both virulent and avirulent strains were employed, the latter in large doses. It was

found that either strain used as a living vaccine in appropriate doses protected monkeys against experimental pneumonia due to the same type of pneumococcus. And a certain amount of cross immunity is conferred by vaccination with cultures of pneumococcus type i. This method is not without its dangers, as a severe and even fatal pneumococcus septicemia frequently followed the use of a vaccine made from virulent pneumococci. It is noteworthy, too, that the active immunity against pneumococcus produced by this method of vaccination, appeared to be independent of the presence or absence of agglutinins or protective bodies in the serum. The animals which recovered from experimental pneumococcus pneumonia were tested for the degree of active immunity conferred by the disease itself (vi, *Jour. Exper. Med.*, 1920, xxxi, 685), by a second intratracheal inoculation. It was found that a high degree of immunity against the homologous type had been obtained, but that little protection was afforded against other types. As regards type iv pneumococcus pneumonia there was no appreciable immunity against the same or homologous strains of pneumococcus type iv. A study was made of the efficacy of type i antipneumococcus serum in the treatment of monkeys with experimental type i pneumococcus pneumonia (vii, *Jour. Exper. Med.*, 1920, xxxii, 1). It was found that intravenous injection of this serum promptly and permanently cleared the blood of pneumococci, shortened the course of the disease, and greatly modified its severity. Better results were obtained when the serum was administered early and at frequent intervals. When the serum treatment was started later in the course of the disease it was found necessary to continue the injections of the serum over a longer period. It is worth while to note that the control animals in these experiments all died and, further, that normal horse serum exerted no beneficial effect. Since particular interest attaches to the pathology of hemolytic streptococcus pneumonia following recent epidemics of this disease, Blake and Cecil considered that it would be of value to attempt the experimental production of this type of pneumonia (viii, *Jour. Exper. Med.*, 1920, xxxii, 401). The same method of experimental infection was carried out, but as the hemolytic streptococcus is much less virulent for monkeys, it was necessary to use a larger dose of organisms, the organisms from 0.1 c.c. to 10 c.c. of an eighteen-hour plain broth culture being suspended in 1 c.c. of fluid for intratracheal injection. Pneumonia was consistently produced in normal monkeys by this method and it had characters comparable with those of hemolytic streptococci pneumonia in man in respect to the clinical history, complications and pathology; that is, an interstitial pneumonia and a confluent lobular pneumonia were both encountered and were frequently found in the same animals. The type of pneumonia appeared to be dependent upon the amount of streptococcus culture injected, since with the injection of a small amount of culture the interstitial type was produced while the confluent lobular type followed the injection of a large amount of culture. The former was characterized pathologically by a cellular reaction, chiefly of mononuclear type in the framework of the lung. The blood remained sterile. The latter, following the injection of the organisms from 5 c.c. or more of culture, showed a confluent lobular distribution of the pneumonic exudate with areas of lax consolidation. There was a mononuclear cell reaction, and a proliferation of fibroblasts and alveolar

epithelium. With very large doses the tissue showed less evidence of resistance. The pneumonia had a lobular distribution, but the areas of exudate were widespread and confluent and the lung tissue involved showed all grades of reaction from edema to consolidation. The striking point of difference between this and pneumococcus pneumonia is seen in the power of the streptococcus to produce marked local injury to the tissue resulting in extensive damage to the walls of the bronchial tree and in widespread areas of alveolar necrosis. Further, as an end-result, there was a tendency for extensive organization to take place. In these cases a terminal invasion of the blood stream by streptococci occurred. The mode of invasion of the lung was the same as with pneumococcus pneumonia, though the type of reaction thereafter had the important differences noted. These writers differ with McCallum in regard to the pathogenesis of streptococcus pneumonia, indicating that the infection invades at or close to the hilum as in pneumococcus pneumonia and is not a primary terminal bronchiolitis. Finally, they found that irritation of the bronchial tree by chlorine gas or lowering of the animal's natural resistance by an intraperitoneal injection of Bacillus influenzæ prior to the intratracheal injection greatly facilitated the invasion of the lungs by Streptococcus hemolyticus. In continuation of the experimental studies of acute respiratory diseases, the effect of inoculation of Bacillus influenzæ into the upper respiratory tract as well as by the intratracheal route next claimed the attention of these investigators. The two final papers of the series (ix, *Jour. Exper. Med.*, 1920, xxxii, 691, and x, *Jour. Exper. Med.*, 1920, xxxii, 719) are devoted to the report of this work. A strain of influenza bacillus isolated from the pleural exudate in a case of pneumonia with empyema following influenza was utilized in this work. The virulence of the culture was raised by passage through a series of mice and monkeys. In those animals in which the nasal mucosa was swabbed with a culture of Bacillus influenzæ an acute respiratory disease followed in most instances. This was of short duration, lasting from three to five days, and was characterized by sudden onset with prostration, the development of sneezing and a cough due to rhinitis and a tracheobronchitis. The febrile reaction was variable and the white blood cell count showed a leukopenia, or sometimes no change. An acute purulent sinusitis was a common complication. In certain of these animals hemorrhagic edema of the lungs, bronchiolitis, and bronchopneumonia also developed. In those receiving the injection of virulent Bacillus influenzæ directly into the trachea, an experimental bronchiolitis and hemorrhagic bronchopneumonia developed in three out of five animals injected. In either type of experimental Bacillus influenzæ infection the influenza bacillus could be recovered by culture in the acute stage either pure or associated with other bacteria. In general, both clinically and pathologically, the processes closely resembled on the one hand simple influenza, and on the other uncomplicated Bacillus influenzæ pneumonia in man. It is noteworthy that experimental Bacillus influenzæ infection can be initiated by a simple swabbing of the nasal mucosa. This indicates a property of invasiveness not possessed by the pneumococcus or by the Streptococcus hemolyticus, as this method of experimental infection with these organisms was shown in the earlier papers to be unsuccessful. Another characteristic difference between Bacillus

influenzæ and pneumococci or Streptococcus hemolyticus infections is seen in the mode of extension in the respiratory system. Inoculated into the upper air passages it extended throughout the mucosal surfaces of these regions, with the result that sinus infections were frequent; here we have another point of resemblance to the disease in man. Further, it was even shown in a number of instances that the simple instilling of cultures of Bacillus influenzæ into the upper air passages also resulted in its extension downward to the finer ramifications, with the development of a terminal bronchiolitis followed by acute inflammatory edema and bronchopneumonia. This mode of spread by continuity along the epithelium of the air passages is in direct contrast to the mode of extension in the case of pneumococcus or Streptococcus hemolyticus, in which the organisms early invade the lymphatics and subsequently extend in these channels. These latter experiments are advanced as evidence in favor of the etiologic relation of Bacillus influenzæ to influenza. As the authors state, it seems reasonable to infer from this work that the influenza bacillus is the cause of influenza. They add, however, that a definite conclusion is not permissible, since it is impossible to determine whether the experimental disease is identical with it or only similar to it.

HYGIENE AND PUBLIC HEALTH

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Investigations of the Germicidal Value of Some of the Chlorin Disinfectants.—TILLEY (*Jour. Agri. Research*, October 15, 1920, No. 2, vol. xx) found that in the ordinary routine work of general disinfection, such as disinfection of cattle cars and pens, there is always a large amount of organic matter present. It is evident, therefore, that because of the enormous diminution in germicidal value on addition of organic matter, as well as because of the injurious effects on metals and fabrics, the chlorin disinfectants, as a class, do not seem to be suited for use under the usual conditions and by the usual methods of general disinfection. That is not to say, however, that when properly used they are not efficient and valuable in the treatment of infected wounds; in fact, the evidence available goes to show that they are of great value when so used; and, of course, chlorin and hypochlorites are being very widely and successfully used for the disinfection of drinking water. Compared on a basis of weight of chloramin-T as against the weight of chlorin, as sodium hypochlorite